Remarks/Arguments

This amendment is in response to the Office Action dated June 17, 2003.

A claim to domestic priority under 35 USC 119(e) is made and has been added to the text as requested.

It is stated that this application does not contain an Abstract as required by 37 CFR 1.72(b). Applicant objects. An abstract was filed with the original PCT application as Page 14, a copy of which is attached in the Appendix. The same Abstract was published as part of the published PCT application. Further, the application as filed was accepted by the Office under 35 USC 371 and 37 CFR 1.494 or 1.495 as being complete on December 31, 2001. As such it is believed that an Abstract already exists in the case and no separate Abstract is required. The Examiner is requested to the Attorney for Applicant if it is still believed that a new Abstract is required.

Claims 1-22 remain in this application. New Claims 23-31 have been added to further delineate the presently claimed invention.

Claims 1 and 2 have been rejected under 35 USC 112 second paragraph as they lack a description of the element that holds the volume of liquid. Amendments have been made to the claims to clarify the existence of one or more wells in a device that hold the volume of liquid. Support for this amendment is found at Page 4, lines 1 and 2 of the specification.

Claim 1 has been amended to include the upper size limitation of 500kD originally contained in Claim 15. Support for this amendment is found at Claim 15 as filed and at page 5, line 30 of the specification.

Claims 7-9,11-13 have been rejected under 35 USC 112 second paragraph as they lack the antecedent basis for the phrase "the device". In view of the amendments to claims 1 and 2, it is believed this rejection has been overcome.

Claims 10 and 14 have been rejected under 35 USC 112 second paragraph as they lack the antecedent basis for the phrase "the plate". They have been amended to the term plate to overcome this rejection.

Claims 10 and 14 have been rejected under 35 USC 112 second paragraph as they are indefinite for failing to show the relationship between the ultrafiltration and the wells in the plate. View of the amendments to claims 1 and 2 it is believed that this relationship is clear in that the filtration occurs in one or more wells.

Claim 15 has been amended to include the upper size limitation of 300kD. Support for this is found in original claim 1 and Page 5, line 31 of the specification.

Claim 16 has been amended to make clear that the range is from about 3kDaltons to about 300kDaltons.

Claims 1,7,15, 17 and 19-21 have been rejected under 35 USC 102(b) by US 4,604,754 (Koyama et al). Applicant disagrees.

Koyama et al relates to the use of a hollow fiber device. Such a device is described in the specification. A hollow fiber device would have minimal surface area available for filtration as compared to a flat sheet membrane. More importantly, it would suffer from a decline in flux and available filtration area as the level of liquid decreases, causing it to have the same flux decay problems as a flat sheet membrane in a centrifugal device. Lastly, Koyama et al is concerned with the recovery of filtrate (note the examples where filtrate recovered is reported) while the present invention

relates to the recovery of the retentate (what is left upstream of the filter). Koyama et al provides no means for the recovery the retentate as is required by the present invention.

As such, it fails to anticipate the present claims.

Claims 1, 7-8,10,15 and 19-21 have been rejected under 35 USC 102(b) over WO 92/13963 (WO'963).

The Office Action states the reference teaches a process for concentrating nucleic acids using an ultrafiltration membrane having a cutoff of 25kD in a single or multiple well plate by adding 'a volume of less 100 microliters of digested DNA mixture sample' and subjecting the sample on a membrane to 'vacuum pressure till RNA are isolated on the membrane ' and cites Figures 1-2, Page 8, lines 4-24; page 13, lines 1-5; page 14, lines 23-30; and page 15 line 15- page 16, line 25.

Applicant finds no teaching for the cited volume of less 100 microliters of digested DNA mixture sample stated in the Office Action and asks for a specific citation from the reference to support that assertion.

The reference generally relates to an apparatus for preparing closed circular DNA and the like. While it does disclose in general the use of vacuum to remove low molecular weight products of proteolytic or nucleolytic digestion and to allow for buffer exchanges, it fails to teach the steps of the present claimed invention. One of skill in the art would not have been taught the present invention as claimed from the teachings of the reference. For example, it fails to each step of the present process. In particular it fails to teach recovering the products from the upper surface of the membrane. Equally, as to the new claims added to the application, it fails to teach filtering the system until substantially all liquid is removed. It fails to teach the claimed vacuum range and it fails to teach that such a process can be used without the need for diafiltration steps to remove salts and the like. One of ordinary skill

in the art in reading the reference would not have filtered to dryness but would have left some residual amount of fluid in the well. They also as is the custom would have conducted one or more diafiltration steps adding buffer, solvent or deionized water to the well to remove salts and the like from the system. Lastly, the examples all appear to use steps such as precipitation or centrifugation at some point in the process.

The present invention allows one to eliminate the need for centrifugation (the reference implies they are equal and can be used as alternatives) and achieve purer samples in equal or less time. This is not taught nor suggested b the reference. As such it fails to anticipate the present claims.

Addressing the specific sections cited as support in the Office Action, Applicant argues that:

Figures 1 and 2 do not support the assertion for which they are cited nor do they anticipate the present claims. Figure 2 in particular is specifically related to the provision of PEG to the bottom of each ultrafiltration membrane which is not required by the present claims.

Page 8, lines 4-24 only cites the use of ultrafiltration by permeation. It fails to teach the use of a constant pressure differential.

Page 13, lines 1-5 states that ultrafiltration may be performed intermittently or constantly but fails to teach how one would run such a process or the force used to cause the filtration. Is it simple permeation as stated at Page 8, lines 4-24 or is it something else that is not stated by the reference?

Page 14, lines 23-30 simply teaches the use of a 25kD membrane to filter a solution containing RNA. Again how one does so is not stated.

Page 15, line 15- page 16, line 25 relates to Figures 1-4. This passage first teaches relative to Figure 1 that PEG or a vacuum may be supplied to the sample holder (lines 25-26) without

anything further. It then states that PEG or a vacuum can be applied to the bottom of a filtration membrane in a sample container (that can be a microtiter plate) so that it constantly removes low molecular weight products of proteolytic or nucleolytic digestion and facilitates buffer exchanges when needed throughout the process.(lines 32-page 16, line2) It then describes Figures 2 and 3 which relate to the use of PEG that is not relevant to the present invention at all. (Page 16,lines 3-17). The cited portions fail to teach the claimed invention.

Claim 5 has been rejected under 35 USC 103(a) over Koyama et al. Koyama fails to teach or suggest any specific pressure at which its invention works. Claim 5 claims a preferred range of pressures for driving the filtration efficiently without adversely affecting the membrane or the product being filtered. This is something not taught nor suggested by the reference. In fact the reference suggests using a hand operated syringe, the pressure applied by such a device would not be constant but would vary from one sample to the next and even within the same sample. As such it would not have been obvious to one of skill in the art to select the use of a range of constant pressures within which to work. The reference by its very nature would allow one to do so.

Claim 3 is rejected under 35 USC 103(a) over WO'963. Claim 3 claims a preferred range of vacuum for driving the filtration efficiently without adversely affecting the membrane or the product being filtered. This is something not taught nor suggested by the reference. In fact, the reference is completely silent as to what level of vacuum to use at all. One would most likely pick a vacuum level well below the minimum range of the claim as the reference suggests filtration by permeation, a rather slow filtration process. As such it would not have been obvious to one of skill in the art to select the use of a preferred range of constant vacuum within which to work.

Claim 9 is rejected under 35 USC 103(a) in view of WO '963 in view of Clark et al. It is stated that it would have been obvious to use the 96 wells of Clark in the WO'963 system.

For there to be a combination there must be some motivation for combining the references other than the teachings of the present invention. Applicant finds no such motivation here. Clark is concerned with assays and reactions and needs to maintain a liquid in a well for "hours or even days" (Column 1, line 35). Gravity and capilliary action tend to cause a loss of liquid. Clark overcomes this through the use of a spout design attached to the bottom of each well. There is no motivation for one to look to Clark to determine the number of wells for the WO 963 application. Even if one did somehow look to Clark, the claim is dependent on an independent claim which not taught by the references and thus this claim is not taught or suggested by their suggested combination as well.

Claims 2, 4, 6, 11-14, 16, 18 and 22 are indicated as being allowable if rewritten or amended to overcome the rejections under 35 USC 112. In view of the amendments made and discussed above it is believed that these claims are now in condition for allowance.

Reconsideration and allowance of the remaining claims is respectfully requested in view of the foregoing amendment and remarks.

Respectfully submitted,

John Dana Hubbard

Attorney for Applicants
Reg. No. 30, 465

September 5, 2003
Millipore Corporation
290 Concord Road
Billerica, Massachusetts 01821
Tel.: (978) 715-1265
Fax: (978) 715-1382

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